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Title: Consensus research priorities for paediatric status epilepticus: a Delphi study of health consumers, researchers and clinicians.

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Highlights

- A Delphi process was conducted with experts in paediatric status epilepticus
- 9 consensus high priority questions were identified
- Future research efforts should be directed towards these priority areas.

Abstract and Key Words: (254 words)

Purpose: Status epilepticus (SE) is a paediatric emergency with significant morbidity and mortality. Recommendations beyond first line care are not based on high quality evidence. Emergency physicians and neurologists are key stakeholders in managing this condition. A collaborative, widely consulted approach to identifying priorities can help direct limited research funds appropriately. The objectives of this study are to identify consensus research priorities in paediatric SE among experts and health consumers.

Methods: A three-stage Delphi process was conducted. Paediatric Neurologists and Emergency Physicians in Australia and New Zealand participated. Round one asked participants to generate three research questions important for further research in paediatric status epilepticus. Responses were refined into unique individual questions. Rounds two and three required participants to rate questions on a seven point ordinal scale. Health consumers were invited to participate by providing up to three problem areas that could be addressed by research.

Results: 54 experts and 76 health consumers participated in the process. Nine questions reached our definition of consensus "high priority", 21 questions achieved consensus "low priority" and seven questions did not achieve consensus. High priority areas included second line management including levetiracetam (efficacy, dose and timing), use of third line agents, induction of anaesthesia (timing and best agent), management of focal SE, and indicators of "subtle SE". Consumer priority areas included themes of treatment efficacy, aetiology, and community education.

Conclusion: We identified nine priority research questions in paediatric SE, congruent with the health consumer theme of treatment efficacy. Future research efforts should be directed towards these priority areas.

Key Words: Status epilepticus, consensus, paediatric, seizures

Introduction

Status epilepticus (SE) is the most common childhood neurological emergency and is, with its underlying aetiology, associated with an estimated mortality of 3% and significant morbidity[1, 2] including development of focal neurological deficits, cognitive impairment, behavioural problems or epilepsy[3]. The incidence of paediatric SE is in the order of 20 per 100,000 population at risk[1, 4]. Aetiology and outcomes of SE in children are different from adults[4]; therefore adult evidence is minimally applicable to paediatric settings. An operational definition of SE based on the indication to commence treatment has been proposed for seizures of five minutes or more[5], replacing the "traditional" definition requiring seizures of greater than 30 minutes duration or two or more sequential seizures without full recovery of consciousness between seizures. These concepts have been incorporated into recent clinical trials[6] and conceptually into recent consensus documents[7].

Benzodiazepines are widely used in the first line pharmacological management of SE, supported by good evidence of efficacy, but recommended subsequent management is based on expert opinion, tradition and consensus[8]. Despite the considerable burden of SE, addressing important clinical questions is challenging with single centre studies, and generally requires a collaborative approach with considerable resources and infrastructure[9]. A collaborative, consultative and systematic approach to identify and clarify the immediate research priorities in SE is indicated to ensure limited research funds are directed appropriately. Incorporating stakeholders' perspectives into the development of research priorities might lead to highly engaged researchers and increased likelihood of translating research into clinical practice.

The Delphi technique is a common approach for the solicitation and collation of opinions from experts in a particular field in the development of ideas and priorities. The Delphi technique has been widely used in health sciences research and is appropriate to correlate informed judgements on topics spanning the disciplines of neurology and emergency medicine. Briefly, the technique involves a set of sequential questionnaires, with information from previous responses summarised and fed back to participants[10]. The first round usually consists of open ended questions soliciting specific information about the content of subsequent structured questionnaires. Three to six rounds are usually employed to reach consensus on a topic[10]. The technique has been successfully used to identify research priorities in the field of paediatric neurology[11], paediatrics[12] and paediatric emergency medicine[13, 14].

The perspective of emergency physicians is perhaps historically underrepresented in SE literature and guideline development, despite being responsible for the majority of acute care decisions in SE in many health systems. It is also imperative that health consumers (i.e. patients and families of patients) are represented to ensure that community expectations about research priorities are met.

The primary objective of this study was to use the Delphi technique to achieve consensus on research priorities in the management of paediatric SE among paediatric neurologists and emergency physicians who treat children. A secondary objective was to determine if research priorities identified by experts aligned with priorities identified by health consumers. The results of this study will help determine where to allocate scarce research resources to achieve better outcomes for patients.

Methods

This was an assessment of expert clinician and health consumer opinion via a Delphi survey to identify research priorities for paediatric SE. The survey was conducted with the support of the Australia and New Zealand Child Neurology Society (ANZCNS) and Paediatric Research in Emergency Departments International Collaborative (PREDICT) network.

Participants

Expert participants were paediatric neurologists and emergency physicians in Australia and New Zealand. An invitation to participate was distributed to paediatric neurologists through the ANZCNS by email, explaining the purpose of the study, the expected time commitment, the proposed number of rounds and timelines. Emergency physicians were invited to participate through site representatives of the PREDICT network. Site representatives at PREDICT sites were asked to nominate interested clinicians, and provide email details, to approximate respondent numbers from neurologists to maintain balance and representation of both groups and inclusion of perspectives of non-researchers. Although controversy exists as to what constitutes the ideal number of subjects in a Delphi study[15-18], it has been recommended that one should have 30 experts from any one discipline, or at least 10 per category for different professional disciplines. It has been suggested that increasing a group size beyond 30 does not generally improve results[16]. A total sample of at least 30 respondents was sought, allowing for attrition.

Consumer participants included health consumers with a diagnosis of epilepsy and a prior SE event, as well as their families. Information regarding the study objectives was distributed through Epilepsy Queensland social media webpages, with an explanatory sheet, and a link to participation in the survey.

Study Procedure and Design

Surveys were constructed and distributed electronically via email, using SurveyMonkey[19]. In round one clinical participants were asked to identify research priorities in the field of paediatric SE that they believed was lacking by answering one single open question: *"Thinking about your experience with paediatric convulsive status epilepticus, what are the most important research questions that need addressing"*. The survey allowed for free text responses, and participants were encouraged to submit the research questions in the PICO format (referring to Population, Intervention, Comparison, Outcome). They were given three weeks in which to respond and could submit up to three questions. Non-responders were emailed a reminder at one and two weeks after initial contact. Consumers were asked to provide up to three problem areas associated with paediatric status epilepticus that could/should be addressed by research. Demographic details were collected from both experts and consumers.

Definitions of SE have been somewhat contentious and continue to evolve[7]. In the survey information we defined SE simply as an *"abnormally long seizure"* operationally defined as when emergency treatment should be started e.g. beyond 5 minutes for tonic-clonic SE. Questions concerning "children" referred to ages 1 month to 16 years, and "infants" as ages 1 month to 12 months.

Questions generated by round one were collated into themes, and developed into mutually exclusive research questions using NVivo 11 for Mac (NVivo qualitative data management Software; QSR International Pty Ltd. Version 10, 2014). Analysis of responses to round one used a grounded theory approach and a process of content analysis and open coding to categorize items into themes[17]. The compiled proposed

questions were reviewed and refined by the investigator team and included in round two in a structured questionnaire. The investigator team included experienced paediatric emergency physicians, paediatric neurologists, clinician researchers and methodological expertise. Surveys were pilot tested for face validity on a group of ED physicians and paediatricians and amended as required. In round two participants were asked to rate the perceived priority of each research question using a seven point Likert-type, ordinal scale (Very low priority, low priority, fairly low priority, neutral, fairly high priority, high priority, very high priority). Participants were also encouraged to supply reasoning and further comments.

Round three consisted of the questions from round two that did not reach predetermined criteria for consensus "high" or "low" priority, together with a summary of feedback for each question including scores and text comments to allow responders to reflect on colleagues scores and thoughts. In round three participants were again asked to rate the perceived priority of each research question using the same seven point Likert-type/ordinal scale.

Analysis plan and statistical considerations

Data from round two and three were exported to an excel spread sheet and analysed on SPSS (Ver 20.0, IBM, Armonk, NY, USA). Overall support for group responses to questions were reported as means and standard deviation. Consensus priority was defined as more than 70% of total respondents rating a question as "fairly high priority" or higher[20]. Consensus "non priority" questions were defined as questions where more than half of the respondents rated the questions as "neutral" or lower priority. The pragmatic decision was made to stop the process at three rounds, considering the low likelihood of achieving consensus with further rounds and survey

response fatigue, based on previous work suggesting that additional rounds produce minimal change in opinion[10, 16].

Consumer participants completed a specifically developed questionnaire, and were asked to list three "questions or ideas for research" which they believe are important for children with convulsive status epilepticus. Responses were exported and qualitative thematic analysis was performed using NVivo 11 for Mac (NVivo qualitative data management Software; QSR International Pty Ltd. Version 10, 2014). These are reported separately and assessed for theme concordance with priorities identified by experts.

Ethics and Consent

The study was approved by the Townsville Hospital Human Research Ethics Committee. Consent of experts was implied when participants responded to the survey via the survey portal. Consumers were given the opportunity to discuss participation with a member of the research team at a mutually convenient time if required, and asked to check a box on the survey instrument indicating consent to participate.

Results

Experts

The three round Delphi process was conducted from April to December 2016. The survey remained open for 4 weeks for each round, with ten weeks between rounds for analysis and development of subsequent surveys. Fifty-four experts agreed to participate in the Delphi process and provided questions and valid email address for subsequent rounds. The demographics of "expert" participants are shown in table 1.

Response rates for round two and three were 42/54 (78%) and 44/54 (81%) respectively.

Questions from round one were imported into NVivo, coded and developed into 37 unique questions in seven categories consisting of: first line agents, second line agents, timing of second line agents, induction of anaesthesia/intubation, home and pre-hospital care, investigation of SE, and general issues.

The results of ranking the 37 questions constituting round 2 of the Delphi process are summarised in table S1 (Supplementary appendix) together with the proportion of responses that rated the question as greater or equal to "fairly high priority" or 4 on the scale. Six questions met our definition of high priority consensus (table 3), while 15 questions met our definition for low priority consensus. The remaining 16 questions that did not reach consensus were refined, and with feedback included in the round 3 survey.

In round 3 a further 3 of 16 questions achieved high priority consensus (table 3), and 6 questions reached low priority consensus, and seven questions failed to reach consensus (intermediate priority). Round 2 and 3 responses are summarised in table 4 and S1. In addition to rating the perceived priority of each research question, participants were able to provide comments and additional insights in a free text response. Indicative quotes accompanying questions achieving high priority status are included in table S2.

Health consumers

The consumer survey was made available from August to November 2016 and received 76 responses. Demographics of health consumer participants are shown in

table 2, and included people with epilepsy and family members of people with epilepsy; a high proportion had previous experience of status epilepticus. Over 100 questions or ideas were generated by the consumer survey. The most common themes included drug therapies and treatment efficacy, causes and "triggers", and outcomes and prognostication (table 4). Less common themes (six responses) concerned medicinal cannabis and education of public and community in general.

Discussion

The Delphi consensus process involving expert emergency physicians and paediatric neurologists identified nine priority research questions for the management of paediatric status epilepticus. Three questions specifically concerned the use of levetiracetam, another concerned the timing of "second line agents" including levetiracetam, and two questions referred to induction of anaesthesia. These were broadly congruent with the "drug therapies" priority theme commonly identified by health consumers. Other questions concerned clinical indicators of subtle SE and management of focal SE.

Experts prioritised a comparative efficacy and safety study between levetiracetam and phenytoin in both infants and children (table 3, questions 1 and 2). Many were aware that studies to address this issue were underway in Australia and New Zealand, the United States and the United Kingdom[21, 22]. This finding confirms that these results are keenly anticipated, and are likely to affect management algorithms internationally.

A separate research question that may not be adequately addressed by current trials was for the most appropriate dose of levetiracetam (table 3, question 7). Current trials are investigating doses of 40mg/kg to 60 mg/kg of levetiracetam[21, 22]. Of interest, pre-hospital use of levetiracetam was not considered a research priority (intermediate

priority) and second line usage of sodium valproate was of low consensus priority in round three. This may reflect unfamiliarity of the drug due to limited availability of the intravenous formulation in Australia and New Zealand, or concerns about safety in certain subpopulations, particularly infants. Again, it is likely that on-going trials will address this question in children older than two years. Other "newer" second line agents such as lacosamide were not proposed as priority research questions in our study.

Another research priority was the use of second line agents, such as levetiracetam earlier in the algorithm (table 3, question 4). This has been advocated by some experts in the literature, including "combination" therapy, and may be facilitated if agents associated with less side effects (e.g. levetiracetam, sodium valproate, lacosomide) are found to be non-inferior to standard therapies. A trial in adults did not demonstrate benefit of the addition of levetiracetam to clonazepam in adult patients with SE in a pre-hospital trial in France[23].

Identifying clinical indicators of subtle SE when electroencephalogram (EEG) is not available was also identified as a high priority question (question 5, table 3). Differentiating ongoing subtle SE from the postictal state can create difficulty in the acute setting, especially in children who may have baseline abnormal neurological function. EEG support in this setting is limited by access to urgent EEG, and the time taken to set up a recording. There are potential adverse consequences from under or over diagnosis of subtle SE (such as excessive SE treatment including intubation, and later long term medication and lifestyle restrictions advice that are based on the reported duration of seizure). Some respondents commented that there were perhaps no reliable clinical indicators of subtle SE. Other respondents, however, commented that increasing expert support at the point of clinical decision making regarding subtle

SE, through review of the patient by experts in subtle SE (by acute video review or neurologist telemedicine consultation) could address this problem, at least in a proportion of SE cases.

Management of focal SE and whether algorithms should be similar to convulsive SE was also a high priority (table 3, question 6). While recent consensus documents have indicated that different operational time frames are applied to focal SE to tonic-clonic SE, it was conceded that this was based on limited data[7]. Our results indicate that clinicians require further clarity in terms of management strategies in this area and may warrant further study.

Induction of anaesthesia was also a high priority area for clinicians (table 3, questions 3 and 8). Whether early induction of anaesthesia improved outcomes achieved consensus with high levels of support, but divided opinion in comments with some suggesting it may be unethical (Table S2). Other experts commented that their clinical experience suggests practice in this regard is already highly variable, as indicated in observational data therefore it is valid to pursue this as a research priority. Conversely, the use of third line agents rather than induction of anaesthesia, a strategy that observational trials suggest is commonly used was also found to be a research priority (table 3, question 9). Additionally, the preferred induction agent was identified as a high priority in round three of the process, with a lack of quality evidence cited. An attempt to investigate this question in adults, comparing Propofol to Barbiturates failed to demonstrate a difference, but this was predominantly due to poor recruitment and early closure of trial[24]. A similar study in children may prove equally difficult, and perhaps methodologies other than RCTs may be required initially. Use of Ketamine and Propofol in the non-intubated patient were both judged to be low priority questions, although proponents may argue they may have a role in

specific circumstances e.g. when it is highly desirable to avoid intubation as with frequent recurrent SE.

In 2014 the U.S. Pediatric Status Epilepticus Research Group (pSERG) published a report summarizing the evidence of paediatric SE and refractory convulsive SE[9]. Based on their literature review, the group identified several knowledge gaps including risk factors for SE, biomarkers, second and third line treatment options and long-term outcome[9]. While the methods used by pSERG differed from our consensus Delphi approach, and knowledge gaps do not necessarily equate with research priorities, the congruence with priorities identified in our study reinforce the importance of our findings.

There were some differences between consumer and expert responses. Apart from the theme of treatment efficacy, consumer priority themes included "triggers" or causes, prognosis as well as medicinal cannabis and education. Differences may be partly explained by unique perspectives on SE. For example emergency physicians may be less likely to consider preventative strategies, however these are clearly no less valuable. The themes identified by consumers are illustrative of the issues important to people and their families affected by epilepsy, and future work can build on these ideas.

Our study had strengths and limitations. The Delphi process is widely used in health sciences.[11-14] The major benefits of the technique are to avoid the limitations of using less formal techniques to achieve consensus such as through committees and panels, which can be prone to domination by powerful individuals and influenced by personalities. The benefits of anonymity and confidentiality contribute to the

development of true expert consensus[17, 20]. Other advantages include that the process allows participants to generate additional insights and more thoroughly clarify information. Other methods of generating consensus opinions, and generating research priorities have been used, and include the Nominal Group Technique and the Hanlon Prioritisation Process[13, 25-27]. The Delphi approach was considered the most appropriate in our circumstance, as experts were geographically dispersed and were not required to physically meet.

Limitations of our study included that our process of identifying and defining expert panellists for the sampling frame was somewhat subjective, and the Delphi technique works on the assumption that participants are equal in knowledge and experience, which may not be correct. However, involvement of emergency physicians and paediatric neurologists in this process was a strength of the design. A further concern is that minority opinion might be lost, and yet still have value. Participants had the opportunity to add comments that were handled in a qualitative analysis of responses. We do not contend that just because a research question did not achieve a consensus high priority by our process, that it is without value or incapable of contributing important knowledge or benefit to patients.

While a strength of the study was the inclusion of health consumers, our methods may have introduced some selection bias. Respondents identified through epilepsy support organisations likely represent patients with more severe or burdensome established epilepsy, only a subgroup of the children presenting with SE. This may have lead to some bias towards responses specific to chronic epilepsy and may account for differences in responses from experts. We did not seek the consensus of consumers through classic Delphi technique in this group, rather evaluated concordance with the consensus of experts.

There is no "gold standard" for defining consensus during a Delphi process, and various definitions have been proposed[17, 20]. Methods used in our study had been advocated and used in similar studies[11, 15, 16, 20]. Further limitations are inherent with any research involving surveys and rating scales include the central tendency bias, where participants tend to avoid rating at the extremes of the scales, acquiescence bias and social desirability bias.

Finally, in our instructions to participants we specifically excluded the neonatal period, for similar reasons that adult SE was excluded. In these age groupings SE was considered to have different aetiologies and outcomes, therefore results of this study are not applicable to the neonatal population. This research only involved participants in Australia and New Zealand, a region with an advanced health system, with high standards of education and training, therefore results should be generalizable to other developed countries.

In summary, we sought to achieve consensus on research priorities in the management of paediatric SE. Our consensus process allowed experts to identify nine high priority research questions consisting of second line management including levetiracetam (efficacy, dose and timing), use of third line agents, induction of anaesthesia (timing and best agent), management of focal SE, and indicators of "subtle SE" concordant with consumer priorities. Results of this research should help inform where future research efforts in paediatric SE should be directed.

References

1. Chin RF, Neville BG, Peckham C, Bedford H, Wade A, Scott RC. Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: prospective population-based study. The Lancet. 2006;368(9531):222-9.
2. Raspall-Chaure M, Chin RF, Neville BG, Scott RC. Outcome of paediatric convulsive status epilepticus: a systematic review. The Lancet Neurology. 2006;5(9):769-79.

3. Novorol CL, Chin RF, Scott RC. Outcome of convulsive status epilepticus: a review. Archives of disease in childhood. 2007;92(11):948-51.
4. Chin R, BGR. N, RC. S. A systematic review of the epidemiology of status epilepticus. European Journal of Neurology. 2004;11:800-10.
5. Lowenstein DH, Bleck T, Macdonald RL. It's time to revise the definition of status epilepticus. Epilepsia. 1999;40(1):120-2.
6. Chamberlain JM, Okada P, Holsti M, Mahajan P, Brown KM, Vance C, et al. Lorazepam vs diazepam for pediatric status epilepticus: a randomized clinical trial. Jama. 2014;311(16):1652-60.
7. Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, et al. A definition and classification of status epilepticus - Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia. 2015 Sep 4. PubMed PMID: 26336950.
8. Appleton R, Macleod S, Martland T. Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children. The Cochrane Library. 2008.
9. Sanchez Fernandez I, Abend NS, Agadi S, An S, Arya R, Carpenter JL, et al. Gaps and opportunities in refractory status epilepticus research in children: a multi-center approach by the Pediatric Status Epilepticus Research Group (pSERG). Seizure. 2014 Feb;23(2):87-97. PubMed PMID: 24183923.
10. Okoli C, Pawlowski SD. The Delphi method as a research tool: an example, design considerations and applications. Information & management. 2004;42(1):15-29.
11. McIntyre S, Novak I, Cusick A. Consensus research priorities for cerebral palsy: a Delphi survey of consumers, researchers, and clinicians. Developmental Medicine & Child Neurology. 2010;52(3):270-5.
12. Rudolph S, Hiscock H, Price A, Efron D, Sewell J, South M, et al. What research questions matter to Australian paediatricians? National Delphi Study. Journal of paediatrics and child health. 2009 Dec;45(12):704-10. PubMed PMID: 19863713.
13. Deane H, Krieser D, Cheek J, Babl F, Dalziel S, Craig S, et al., editors. Predict Delphi Study: Establishing The Research Priorities Of Paediatric Emergency Medicine Clinicians In Australia And New Zealand. 32nd Annual Scientific Meeting of the Australasian College for Emergency Medicine (ACEM-ASM 2015); 2015 22 – 26 November; Brisbane.
14. Hartshorn S, O'Sullivan R, Maconochie IK, Bevan C, Cleugh F, Lyttle MD. Establishing the research priorities of paediatric emergency medicine clinicians in the UK and Ireland. Emergency Medicine Journal. 2015:emermed-2014-204484.
15. Crisp J, Pelletier D, Duffield C, Adams A, Nagy S. The Delphi Method? Nursing Research. 1997;46(2).
16. De Villiers MR, De Villiers PJ, Kent AP. The Delphi technique in health sciences education research. Medical teacher. 2005;27(7):639-43.
17. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. Journal of advanced nursing. 2000;32(4):1008-15.
18. Hsu C-C, Sandford BA. The Delphi technique: making sense of consensus. Practical assessment, research & evaluation. 2007;12(10):1-8.
19. SurveyMonkey Inc. San Mateo, California, USA. Available from: http://www.surveymonkey.com.
20. Keeney S, Hasson F, McKenna H. Consulting the oracle: ten lessons from using the Delphi technique in nursing research. Journal of Advanced Nursing. 2006;53(2):205-12.
21. Emergency Treatment with Levetiracetam or Phenytoin in Status Epilepticus in Children (EcLiPSE) – an open label randomised controlled trial (Protocol) Clinical Trials Research Centre: National Institute for Health Research; [cited 2017 Jan 10]. Available from: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0014/123350/PRO-12-127-134.pdf.

22. Bleck T, Cock H, Chamberlain J, Cloyd J, Connor J, Elm J, et al. The established status epilepticus trial 2013. Epilepsia. 2013 Sep;54 Suppl 6:89-92. PubMed PMID: 24001084. Pubmed Central PMCID: 4048827.
23. Navarro V, Dagron C, Elie C, Lamhaut L, Demeret S, Urien S, et al. Prehospital treatment with levetiracetam plus clonazepam or placebo plus clonazepam in status epilepticus (SAMUKeppra): a randomised, double-blind, phase 3 trial. The Lancet Neurology. 2016;15(1):47-55.
24. Rossetti A, Milligan T, Vulliémoz S, Michaelides C, Bertschi M, Lee J. A randomized trial for the treatment of refractory status epilepticus. Neurocrit Care. 2011;14(1):4-10.
25. Keijzers G, Thom O, Taylor D, Knott J, Taylor DM, Clinical Trials Group ACfEM. Clinical research priorities in emergency medicine. Emergency medicine Australasia : EMA. 2014 Feb;26(1):19-27. PubMed PMID: 24118984.
26. Miller SZ, Rincon H, Kuppermann N, Pediatric Emergency Care Applied Research N. Revisiting the emergency medicine services for children research agenda: priorities for multicenter research in pediatric emergency care. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2008 Apr;15(4):377-83. PubMed PMID: 18370994.
27. Thom O, Keijzers G, Davies S, Mc DTD, Knott J, Middleton PM. Clinical research priorities in emergency medicine: results of a consensus meeting and development of a weighting method for assessment of clinical research priorities. Emergency medicine Australasia : EMA. 2014 Feb;26(1):28-33. PubMed PMID: 24495058.

Table 1. Demographic details of respondents to expert survey.

	n (%)
Gender	
Female	21 (39%)
Age Range	
25-34	1 (2%)
35-44	26 (48%)
45-54	20 (37%)
55+	7 (13%)
Years since medical graduation	
Median 21 (IQR 16 to 26)	
Speciality	
Emergency physician	22 (41%)
Paediatric Neurologist	32 (59%)
Hospital category	
Tertiary	43 (80%)
Secondary	5 (9%)
Both	6 (11%)
Full time / Part time	
Full time	39 (72%)
Part time	15 (28%)

IQR interquartile range, all

Table 2. Demographic details of respondents to consumer survey.

	n (%)
Gender	
Female	68 (89%)
Age Range	
18-24	7 (9%)
25-34	13 (17%)
35-44	27 (35%)
45-54	16 (21%)
55+	13 (17%)
Highest level of education attained	
School certificate (Year 10)	12 (16%)
Higher school certificate (Year 12)	13 (17%)
Post school, non-university	23 (30%)
Undergraduate university degree	20 (26%)
Postgraduate university degree	8 (11%)
Religious preference	
Christianity	42 (55%)
No religion	33 (43%)
Islam	1 (1%)
Approximate annual household income	
Less than $25K	14 (18%)
$25-49K	15 (19%)
$50-74K	14 (18%)
$75-100K	15 (19%)
More than $100K	18 (24%)
Diagnosis of epilepsy	
Self	34 (45%)
Child	37 (49%)
Sibling	2 (3%)
Previous episodes of status epilepticus	
Yes	58 (76%)

Table 3. Consensus high priority questions, rankings and scores.

Questions	Round 2		Round 3	
	% ≥ 4*	Mean (SD)	% ≥ 4*	Mean (SD)
1. In **infants** with convulsive SE, is levetiracetam superior to phenytoin (or phenobarbitone) for efficacy (seizure termination) and safety (adverse effects)?	85%	5.3 (1.1)		
2. In children with convulsive SE, is levetiracetam superior to phenytoin for efficacy (seizure termination) and safety (adverse effects)?	82%	5.5 (1.3)		
3. In children with convulsive SE is the early use of anaesthesia associated with more rapid seizure terminations, less complications and better long-term outcomes, compared to anticonvulsant treatment alone?	82%	5.2 (1.2)		
4. In children with convulsive SE, is earlier administration of a second line agent (e.g. levetiracetam) more effective than standard protocols?	74%	4.9 (1.1)		
5. If EEG is not available, what are the most reliable clinical indicators of ongoing subtle SE?	73%	4.9 (1.4)		
6. In children with focal SE should the medical management proceed according to similar treatment pathways as for convulsive SE, and within the same time frames?	72%	4.7 (1.1)		
7. In children with convulsive SE, what is the most appropriate dose of levetiracetam as a second line agent?	68%	5.0 (1.2)	77%	4.9 (1.2)
8. In children with convulsive SE who require intubation, what induction agent is most effective for seizure termination, long-term outcome and complications (e.g. ketamine, propofol, thiopentone, other)?	68%	4.8 (1.1)	81%	5.1 (1.2)
9. In children with convulsive SE, Is third line medical anticonvulsant drugs compared with induction of anaesthesia and intubation associated with improved long-term outcomes?	66%	4.9 (1.2)	81%	5.1 (1.0)

*Denotes percentage of respondents who ranked question fairly high priority (4 on scale) or higher. SD standard deviation.

Table 4. Consumer survey data. Common themes, counts and indicative quotes.

Drug Therapies and treatment efficacy (20 references) *"optimal agent /timing"* *"Most effective treatment"* *"maximal safe pre-hospital care"* *"A simpler easy to use rescue medication as an alternative to what is available if available meds don't work."*
Causes and Triggers (19 references) *"What causes it"* *"Research the triggers and warning signals to help parents be proactive in preventing status episodes from occurring."* *"What are the major triggers for CSE?"*
Outcomes and prognosis (18 references) *"What are the long term cognitive effects of these episodes?"* *"Neuropsych testing for school performance"* *"What harm can occur"*
Medicinal cannabis (6 references) *"Would medically approved marijuana help"* *"get cannabis oil legalised not just for children"*
Education (3 responses) *"More education for nursing and other medical staff on how to deal with status episodes"* *"Community education around responding to status epilepticus for non-primary carers"*